Case Report Rapport de cas

Successful treatment of *Solanum dulcamara* intoxication in a Labrador retriever puppy

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Abstract — A 10-week-old intact male Labrador retriever dog was presented for acute onset of weakness, ataxia, and generalized muscle tremors. The puppy was suffering respiratory and central nervous system (CNS) depression, was mildly pyrexic, and vomited plant material that was identified as creeping nightshade *(Solanum dulcamara)*. He responded well to supportive care and was discharged successfully. To the authors' knowledge, this is the first report of *Solanum dulcamara* toxicity occurring in a dog.

Résumé — Traitement réussi d'une intoxication par *Solanum dulcamara* chez un chiot Labrador retriever. Un chien Labrador retriever mâle intact âgé de 10 semaines a été présenté pour l'apparition aiguë de faiblesse, d'ataxie et des tremblements musculaires généralisés. Le chiot souffrait d'une dépression du système respiratoire et du système nerveux central (SNC), présentait une pyrexie légère et vomissait du matériau végétal qui a été identifié comme étant de la morelle douce-amère *(Solanum dulcamara).* Il a bien répondu à des soins de soutien et a reçu un congé pour un traitement réussi. À la connaissance des auteurs, c'est le premier rapport d'une toxicité de *Solanum dulcamara* se produisant chez un chien.

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Solanum dulcamara is a nightshade plant known as bittersweet nightshade, creeping nightshade, or woody nightshade (1). It has dark green leaves, star-shaped purple flowers with backward pointing petals, and a large yellow stamen at the center (Figure 1) (2). The berries are ovoid and change from green to red as they ripen (Figure 1) (2). This plant is native to Europe, Asia, and northern Africa, it is naturalized in the United States, and is often considered an invasive weed species (2). About 1500 species of *Solanum* exist worldwide (1). *Solanum* spp. toxicosis has been reported in children, horses, and livestock, but published reports in small animals are lacking (4–10).

The toxic principle of *Solanum dulcamara* is the steroidal glycoalkaloid solanine (3). Following ingestion, solanine is poorly absorbed from the gastrointestinal (GI) tract causing local irritation and clinical signs of hypersalivation, vomiting, diarrhea, and ileus (1). In the GI tract, solanine is also hydrolyzed to solanidine, which is absorbed and produces the systemic toxidrome of neurologic, cardiovascular, and respiratory signs (1). Reported signs include mydriasis, central nervous system depression, muscle tremors, incoordination, tachycardia or bradycardia, and respiratory difficulty (1). Neurologic signs result from direct neurotoxic effects of solanidine in addition to acetylcholinesterase inhibition (3). Due to its similarities to cardiac glycosides, solanine and solanidine also have positive inotropic effects (8).

The amount of toxin present in various parts of the plant depends on the climate, soil, amount of light, and season, but in general, the unripe fruit and leaves are most toxic (1–3). Gastric and small intestinal epithelial necrosis was noted in Syrian hamsters fed unripe fruit from *Solanum dulcamara* and 8 of 10 died (11). There were no signs of toxicity or histologic changes in mice gavage fed ripe berries from early summer, while those fed unripe berries from early summer had histologic changes without toxicity and those fed unripe berries from later in the summer had signs of toxicity but few histologic changes, suggesting that toxicity of the berries can vary seasonally (12). Experimental studies have also shown a wide variety of tolerance to the amount of toxin delivered depending on the species of animal (8). For instance, oral doses of solanine at 3 mg/kg body weight (BW) produce clinical signs of dyspnea, drowsiness, and hyperesthesia in humans, 20 to 35 mg/kg BW is lethal in rats and rabbits, whereas oral doses of 225 mg/kg BW are not lethal in sheep (8).

The objective of this report is to describe the clinical course and successful treatment of confirmed *Solanum dulcamara* toxicity in a dog.

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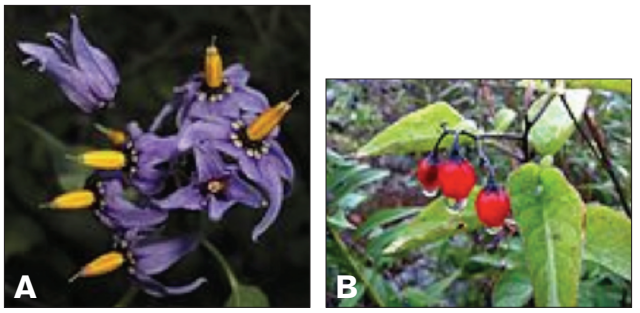

Figure 1. *Solanum dulcamara* (A) flowers, (B) leaves and berries.

Table 1. Serial venous blood gas values in a Labrador retriever puppy following hospitalization for ingestion of *Solanum dulcamara*

Measured parameter (reference interval)	Time (hours) following initial venous blood gas			
	T0	T10	T34	T58
PCO_2 (35 to 45 mmHg)	47.9	68.3	39.4	43.9
HCO_3 (18 to 25 mmol/L)	26.4	30.1	26.2	28
pH (7.33 to 7.45)	7.36	7.26	7.44	7.42
BE (−2 to 2)	0.9	3.0	2.1	3.5
Na (139 to 151 mmol/L)	140.5	137.5	138.1	137.4
K (3.8 to 5.3 mmol/L)	4.85	4.13	4.44	4.41
Cl (102 to 120 mmol/L)	107.3	100.9	105	101.8
iCa (1.12 to 1.42 mmol/L)	1.33	1.49	1.42	1.48
Glucose (77 to 150 mg/dL)	167	145	106	152

PCO_2 — partial pressure of CO_2; BE — base excess.

Case description

A 10-week-old intact male Labrador retriever puppy weighing 6 kg was presented to the emergency department of a private referral hospital in Massachusetts, USA in the spring with an acute onset of weakness, ataxia, and muscle tremors. He had been in a crate with his sibling for several hours prior to the observed clinical signs. The puppy had previously been healthy, and the sibling was not exhibiting any clinical signs. His vaccination status was current for a dog of his age.

On physical examination at the time of presentation, he was mentally obtunded and recumbent with generalized muscle tremors. He was pyrexic (rectal temperature: 39.7°C), tachycardic (heart rate: 160 beats/min), and tachypneic (respiratory rate: 50 breaths/min), with a short, shallow respiratory pattern. His cranial nerve responses were intact. An initial venous blood gas analysis revealed a mild hypercapnia at 47.9 mmHg [reference range (RR): 35 to 45 mmHg], with mild hyperglycemia and normal electrolyte concentrations (Table 1, T0). A complete blood (cell) count and full biochemistry panel revealed a mild anemia (Hct: 26.5%) and hypoproteinemia (total protein 38 g/L), consistent with the patient's age. The patient vomited normal ingesta and plant material shortly thereafter so was given maropitant (Cerenia; Zoetis, Florham Park, New Jersey, USA), 1 mg/kg BW, SQ. The owner did not recognize the plant material (dried stems and unripe berries), but the following morning, a photograph of it was sent to a local botanist who identified it as *Solanum dulcamara.* The owner subsequently found the plant in his backyard (Figure 2) where the puppy could have had access to it.

Figure 2. Plant material from patient's yard that was consistent with plant material that he vomited.

Initial treatment included administration of flow-by oxygen, IV administration of Lactated Ringer's Solution (25 mL/kg BW bolus followed by 5 mL/kg BW/h infusion), diazepam (Valium; Hospira, Lake Forest, Illinois, USA), 0.5 mg/kg BW, IV and methocarbamol (Robaxin; West-Ward Pharmaceuticals, Eatontown, New Jersey, USA), 55 mg/kg BW, IV. No improvement in tremors was noted, so midazolam (Hospira) as a continuous rate infusion (CRI) at 0.5 mg/kg BW per hour, IV, was started. The tremors subjectively worsened with this therapy, so it was discontinued after 15 min. A bolus dose of propofol (PropoFlo; Abbott, Abbott Park, Illinois, USA), 20 mg, IV was given, and the patient's tremors ceased. A 60-mL (10 mL/kg BW, per rectum) warm water enema was administered to further decontaminate the gastrointestinal (GI) tract but did not result in a bowel movement.

Tremors resumed several minutes after the initial dose of propofol had been administered. The ASPCA Poison Control Center, Urbana, Illinois, USA, was consulted although the plant had not yet been identified. A tremorgenic toxin was suspected and, therefore, a higher dose of methocarbamol (100 mg/kg BW, IV) was recommended and administered. The tremors improved after this dose but were still present. Further consultation with the poison control center was sought, and phenobarbital (West-Ward Pharamceuticals), 4 mg/kg BW, IV, was given as recommended. Tremors were lessened further with this; however, the patient became even more sedate. The dog's temperature had normalized at this time (38.6°C) but the central nervous system (CNS) depression and vomiting caused concern for potential aspiration. We decided to intubate the puppy, so another dose of propofol, 2 mg/kg BW, IV, was given. Anesthesia was maintained with a propofol CRI at 0.2 mg/kg BW/min, IV, a midazolam CRI at 1 mg/kg BW per hour, IV, and isoflurane gas at 1% in 100% oxygen at a flow rate of 1 L/min. The isoflurane was discontinued after 30 min, and anesthesia was maintained with propofol and midazolam. Oxygen was provided via flow-by through the endotracheal tube (ET). Gastric lavage was attempted, but the orogastric tube was too narrow to allow passage of material through it.

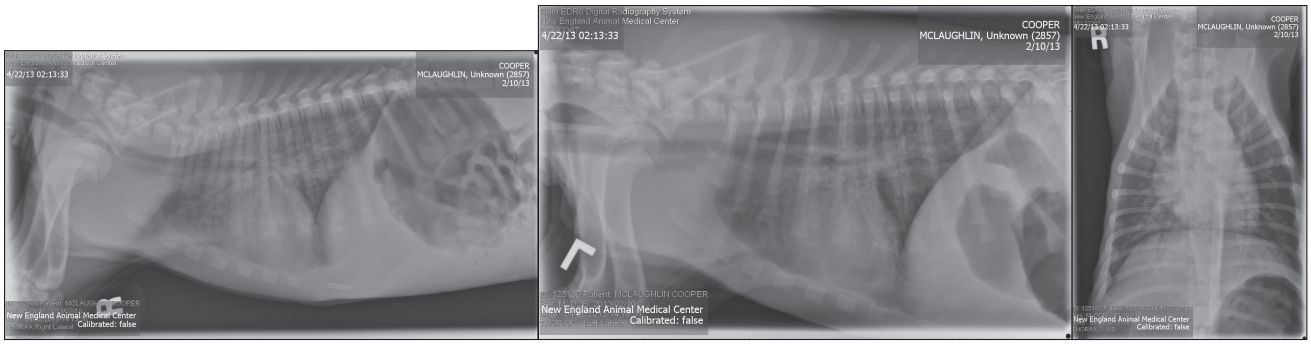

Figure 3. Three view thoracic radiographs taken after final extubation. Diffuse interstitial infiltrates are noted on both lateral projections, but not as evident on the ventro-dorsal view. These changes may represent some degree of atelectasis from anesthesia. There is air distension of the esophagus, which is most evident on the left lateral view and is suspected to be due to post-anesthetic recovery. There are no dependent alveolar consolidations to suggest aspiration pneumonia, but the films were taken shortly after extubation, and, therefore, it may be too early in the disease process to be radiographically evident.

A multi-parameter unit (SurgiVet; Smiths Medical, Dublin, Ohio, USA) was used to facilitate continuous monitoring of the dog's electrocardiogram (ECG), pulse oximetry (SPO_2), and oscillometric blood pressure. Ongoing IV fluid therapy was provided at 30 mL/h of isotonic crystalloid. The patient continued to breathe on his own and did not receive positive pressure ventilation; however, he did have mild episodes of hypotension which required adjustments in the rate of the propofol CRI and boluses of crystalloid and colloid. He also became hypothermic under anesthesia, so a forced air heating blanket was provided. Recheck blood gas analysis approximately 10 h after the initial database showed a more severe hypercapnia with respiratory acidosis, mild hypochloremia, and mild ionized hypercalcemia (Table 1, T10). The patient was given intermittent positive pressure ventilation by hand to normalize the hypercapnia.

Approximately 10 h after intubation the dog was weaned from anesthesia by gradual reductions in the rates of the propofol and midazolam CRIs over the course of an hour. In preparation for extubation, the cuff of the endotracheal tube had been deflated, but the tube was still in place when the patient vomited clear phlegm. The tube was re-inflated and the oral cavity suctioned. There was a plug of mucopurulent phlegm at the end of the endotracheal tube when it was removed. The patient was temporarily re-intubated with a sterile endotracheal tube, and an endotracheal wash was performed for cytology and culture. Pulse oximetry was 94% on room air and end tidal CO_2 ($ETCO_2$) was between 37 and 40 mmHg at the time of extubation.

The puppy was recovered in 40% oxygen in an oxygen cage for several hours during which he experienced intermittent, non-productive coughing. He was alert enough to keep himself sternal at this time. Three view thoracic radiographs showed a diffuse, interstitial pulmonary infiltrate but no obvious dependent alveolar consolidations to indicate aspiration pneumonia (Figure 3). However, concerns for pneumonia remained due to the prior vomiting, so ampicillin with sulbactam (Unasyn; Auromedics, Dayton, New Jersey, USA), 50 mg/kg BW, IV, q8h, was started pending results of the endotracheal wash culture. The tracheal wash cytology showed neutrophilic inflammation, and the culture grew *Escherichia coli* that was susceptible to amoxicillin/clavulanate (Clavamox; Zoetis), both consistent with aspiration pneumonia. That afternoon, a CRI of metoclopramide (Reglan; Hospira) was also started, given reports of *Solanum* species causing gastrointestinal ileus. No additional doses of anti-emetics were needed. Oxygen therapy was discontinued 3 h after final extubation and the patient's pulse oximetry was 96% on room air. Recheck venous blood gas the following morning showed resolution of the previously noted abnormalities (Table 1, T34).

After recovery from anesthesia, tremors did continue, but they were intermittent and minor compared to those on initial presentation. No additional medications were needed to control them. The patient's mental status improved and he was ambulating normally 5 h after final extubation. The following morning, the puppy was bright and alert with normal mentation, and he began eating. Discharge, with complete resolution of clinical signs, occurred approximately 64 h after presentation to the hospital.

Discussion

To the authors' knowledge, this is the first report of *Solanum dulcamara* toxicity in a dog. The clinical signs of GI upset, respiratory depression, and CNS depression in the puppy reported here are similar to those reported in other species with *Solanum* spp. toxicity, including horses, cattle, and children (4–9). These include reports of fatalities in humans and livestock from ingesting *Solanum* species.

In 1 report, 6 horses received poor quality hay containing silverleaf nightshade *(Solanum eleagnifolium)* and white horse nettle *(Solanum dimiditum)*; they had signs similar to those herein, including obtundation, ataxia, pyrexia, muscle fasciculations, and ileus (4). Other signs noted in these horses included urinary retention and cranial nerve deficits; however, these may have been due to concurrent ivermectin toxicosis (4). Therapy in these horses was not well described, but all 6 affected horses recovered (4). The literature also includes cases of *Solanum dulcamara* toxicosis in humans that were fatal (10) and cases that were successfully treated (6). One report documents the case of a child ingesting *Solanum dulcamara* who presented in an anticholinergic crisis with pyrexia, tachycardia, obtundation, and muscle tremors (6). She was treated with the cholinesterase

inhibitor physostigmine and was discharged 36 h later (6). Other reports document *Solanum tuberosum* (potato) toxicosis, associated with high light exposure and increased concentrations of solanine in the plant (8).

Treatment in all reported cases of *Solanum* toxicity has been symptomatic and supportive. In our case, this supportive care consisted of IV fluid therapy, nausea control, prokinetics, and anesthesia to keep the patient intubated to protect the airway. Despite this, the patient did develop aspiration pneumonia. One could consider extubating patients with a partially inflated cuff to try to prevent this from happening in future cases. Also, we could have started the metoclopramide CRI sooner to try and prevent continued GI signs. Given its effectiveness in treating an affected child (6), the cholinesterase inhibitor physostigmine should be considered in future cases of suspected or confirmed toxicosis. The use of methocarbamol was not reported in other cases in the literature and the tremors herein seemed only minimally responsive even at higher doses. The mechanism of action of methocarbamol is not understood, but it does not appear to act on the muscle cells or motor end plates directly so a centrally acting depressant effect is thought to be the main mechanism of action (7). It is possible that the tremors would be responsive to even higher doses than those used in this study, or to a CRI, but it is also possible that methocarbamol is not effective against the tremorgenic effects of solanidine. Other toxins that cause tremors and need to be considered include bromethalin, metaldehyde, mycotoxins, methylxanthines, strychnine, organophosphates, amphetamines, selective serotonin reuptake inhibitors (SSRIs), and albuterol.

Intermittent $ETCO_2$ values were obtained in this patient. Continuous $ETCO_2$ monitoring would have been ideal for comparison to blood gas values and to monitor for hypoventilation and the need for positive pressure ventilation. However, when the patient was noted to have an elevated partial pressure of carbon dioxide (PCO_2), he was treated with manual hand ventilation. An $ETCO_2$ that was checked prior to extubation was normal. Intermittent manual positive pressure ventilation was enough to correct this patient's hypercapnia, but mechanical ventilation could have been considered in light of his obtunded mentation and poor ventilation.

This report describes the first known case and successful treatment of *Solanum* toxicity in a small animal patient. *Solanum* toxicity should be considered as a possible differential in patients presenting with compatible clinical signs where the plant is known to grow, especially in patients with generalized muscle tremors.

Acknowledgment

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